Letters to the Editor

Ischemia-Modified Albumin and Myocardial Ischemia

Sbarouni et al. (1) reported on "Ischemia-Modified Albumin [IMA] in Relation to Exercise Stress Testing [EST]" in a previous issue of the *Journal*. Although the investigators found significant differences in the IMA values at baseline, peak exercise, and after EST, there was no relation between the IMA changes and the result of the EST. The researchers stated that changes in IMA levels do not reflect myocardial ischemia and that IMA does not seem to improve the accuracy of EST. Although these are highly interesting results, some important points must be considered in this study.

Previous studies have shown that IMA is a marker of myocardial ischemia, and it was accepted that IMA is an early marker to help in ruling out patients with acute coronary syndrome (2,3). Interestingly, Sbarouni et al. (1) concluded that IMA levels do not indicate myocardial ischemia different from these other studies. False negative and false positive results of exercise testing are important clinical problems in diagnosis of coronary artery disease (CAD). The sensitivity and specificity of EST range between 60% and 70% (4,5). Approximately 30% to 40% more false negative results may be obtained in clinical practice. Therefore, each positive EST is not accepted as a sign of myocardial ischemia. However, in the study by Sbarouni et al. (1), a positive stress test is accepted as indicative of myocardial ischemia. It is not mentioned how many patients with positive EST have myocardial ischemia. In our opinion, lack of this important information may change the study results.

Other conflicts and controversial subjects are related to results from postexercise IMA levels. Because plasma IMA levels increase within minutes after myocardial ischemia, peak exercise IMA levels may not indicate myocardial ischemia. However, postexercise IMA levels may be helpful to determine myocardial ischemia during exercise. Previously, it was demonstrated that IMA levels decrease after physical exercise, and it was hypothesized that this immediate decrease may have been attributable to interference in the IMA measurement by lactate produced during skeletal muscle ischemia (6,7) However, release of lactate after EST in patients with peripheral vascular disease has been reported (8) Although Sbarouni et al. (1) concluded that a decrease in IMA levels is associated with hemoconcentration, it was unknown whether peripheral vascular disease was present in the study population. Therefore, possible peripheral vascular disease in patients may affect IMA levels via increased lactate concentration.

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REFERENCES

1. Sbarouni E, Georgiadou P, Theodorakis GN, Kremastinos DT. Ischemia-modified albumin in relation to exercise stress testing. J Am Coll Cardiol 2006;48:2482–4.
2. Sinha MK, Roy D, Gaze DC, Collinson PO, Kaski JC. Role of "ischemia modified albumin," a new biochemical marker of myocardial ischaemia, in the early diagnosis of acute coronary syndromes. Emerg Med J 2004;21:29–34.
3. Anwaruddin S, Januzzi JL Jr., Baggish AL, Lewandrowski EL, Lewandrowski KB. Ischemia-modified albumin improves the usefulness of standard cardiac biomarkers for the diagnosis of myocardial ischemia in the emergency department setting. Am J Clin Pathol 2005;123:140–5.
4. Gibbons RJ, Abrams J, Gary J, et al. ACC/AHA guidelines for exercise testing: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Exercise Testing). J Am Coll Cardiol 1997;30:260–311.
5. Sketch MH, Mohiuddin SM, Nair CK, Mooss AN, Runco V. Automated and nomographic analysis of exercise tests. JAMA 1980; 243:1052–5.
6. Apple FS, Quist HE, Otto AP, Mathews WE, Murakami MM. Release characteristics of cardiac biomarkers and ischemia modified albumin as measured by the albumin cobalt-binding test after a marathon race. Clin Chem 2002;48:1097–100.
7. Zapico-Muniz E, Santalo-Bel M, Merce-Muntanola J, Montiel JA, Martinez-Rubio A, Ordonez-Llanos J. Ischemia-modified albumin during skeletal muscle ischemia. Clin Chem 2004;50:1063–5.
8. Duprez D, De Buyzere M, Van Wassenhove A, Clement D. Evaluation of the metabolic compensation after treadmill test in patients with peripheral occlusive arterial disease. Angiology 1992;43:126–33.

Ischemia-Modified Albumin: The Importance of Oxidative Stress

We read with interest the recent study by Sbarouni et al. (1) which adds to the growing body of evidence regarding ischemia-modified albumin (IMA). Interestingly, in their study, the IMA levels dropped significantly at peak exercise in both patients with positive and negative exercise stress-test responses, suggesting that the observed changes in IMA levels may not reflect myocardial ischemia. In addition to Sbarouni et al. (1), other investigators have previously shown reduced IMA levels immediately after exercise in different clinical conditions: for example, exercise-induced skeletal muscle ischemia in patients with peripheral vascular disease (2) and induced forearm ischemia in normal volunteers (3). The possible explanations for the observed IMA changes after exertion include an increase in albumin levels due to hemoconcentration and the resultant decrease in the nonbound portion of cobalt. It has also been suggested that this immediate decrease in IMA concentration may be attributable to interference with the IMA measurement by lactate produced during skeletal muscle work or ischemia. These findings are important for 2 main reasons: 1) they may cast doubt as to whether IMA changes are truly representative of cardiac ischemia in patients with chest pain,